No. 33.—JUNE, 1905

DEPARTMENT OF THE INTERIOR
BUREAU OF GOVERNMENT LABORATORIES
BIOLOGICAL LABORATORY

FURTHER OBSERVATIONS ON FIBRIN THROMBOSIS IN THE GLOMERULAR AND OTHER RENAL VESSELS IN BUBONIC PLAGUE

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LETTER OF TRANSMITTAL.

DEPARTMENT OF THE INTERIOR,
BUREAU OF GOVERNMENT LABORATORIES,
OFFICE OF THE SUPERINTENDENT OF LABORATORIES,
Manila, June 8, 1905.

SIR: I have the honor to transmit herewith and recommend for publication "Further Observations on Fibrin Thrombosis in the Glomerular and Other Renal Vessels in Bubonic Plague," by Dr. Maximilian Herzog, Pathologist, Biological Laboratory.

Very respectfully,

RICHARD P. STRONG,
Director Biological Laboratory,
Acting Superintendent Government Laboratories.

Hon. DEAN C. WORCESTER,
Secretary of the Interior, Manila, P. I.

FURTHER OBSERVATIONS ON FIBRIN THROMBOSIS IN THE GLOMERULAR AND OTHER RENAL VESSELS IN BUBONIC PLAGUE.

By Maximilian Herzog, M. D., *Pathologist Biological Laboratory.*

A short time ago the writer called attention to the frequency of hyaline fibrin thrombi in the glomerular capillaries and in other renal vessels in bubonic plague. In the introduction to Bulletin No. 23, Biological Laboratory, Bureau of Government Laboratories, Manila, October, 1904, entitled "The Plague: Bacteriology, Morbid Anatomy, and Histopathology," on page 10 the following reference to these histopathologic changes was made:

> In studying the histopathology of plague a highly interesting change was found in the kidneys, namely, extensive and frequently occurring hyaline fibrin thromboses in the glomerular capillaries. As it appears that this change has not been described in the study of the microscopic anatomy of the disease, it has been considered somewhat at length.

At the time the above was written, the histopathologic change under discussion had been found in seven out of twenty cases examined. When these investigations were undertaken, as was stated in Bulletin No. 23, the important publications of the Austrian Plague Commission were not accessible in Manila. Only after the bulletin was in print did they arrive from Europe. From the Austrian commission's publications it is evident that Albrecht and Gohn had indeed previously encountered the same changes and had even reproduced them in one of their drawings, but it is equally clear that they have entirely misinterpreted and wrongly described them. It is obvious that the material from which the description and illustrations were derived had been improperly fixed, and hence its examination led to the faulty interpretation of the changes which had actually occurred. This interpretation has been repeated again and again and quoted by subsequent writers in the description of the histologic changes in plague. Everywhere do we read of the

hyaline degeneration of the vessel walls, and nowhere are the thrombotic processes clearly and unmistakably described or their frequent occurrence and importance sufficiently emphasized.

Albrecht and Gohn (Vol. II, p. 546, of their report) describe the kidney changes in plague in the following words:[1]

In plague, as in many infectious diseases, the kidneys, both macro- and microscopically, exhibit in a most pronounced manner the signs of parenchymatous and fatty degeneration. Histologically one sees in them not only the changes of cloudy swelling and simple fatty degeneration but also loss of nuclei and necrosis.

Multiple cortical hemorrhages in the shape of typical glomerular hemorrhages are very frequent. In many plague kidneys one finds a very striking glomerular change. The individual capillary loops are transformed into cords (*stränge*), which stain well with eosin, are still sharply differentiated, and which consist of "beam" or thread-like appearing coagula (*gerinseln*). In this manner these glomeruli, deeply stained and well preserved in their shape, contrasting with the remainder of the poorly stained cortex, form a very striking picture. Between such a glomerulus and its capsule there is never any exudate. The vasa afferentia leading to the glomeruli often show the same picture of coagulation (*gerinnungsbilder*), and the latter is not only found in the vascular lumen but also involves the vessel wall. (See Table XI, fig. 1.[2]) In general these pictures are completely identical with those which we observe in multiple splenic foci and in genuine plague pneumonia.

Here also we are dealing with coagulations in the blood, in the tissue juices, in the elements of the vessel wall itself, *which can not be stained according to Weigert's fibrin method*[3] and which when stained by the Van Gieson stain assume a light yellow tint.

Such glomerular changes are found only in such cases in which very numerous bacilli are circulating in the blood. The bacilli then are found densely crowded in the capillaries and small vessels of the cortex and they can also be seen abundantly between the cord- and net-work of the vascular lumina.

Such is the description of the vascular changes of the kidneys as given by Albrecht and Gohn. In this connection we must point

[1] This quotation has been translated from the original as literally as possible.

[2] According to their explanation of the tables, fig. 1, Table XI, a colored drawing, was prepared from material fixed in the Mueller-Orth formalin mixture and then stained with hæmalum and eosin. As stated in another part of the present report, such a method of fixation is absolutely worthless for the microscopic study of the thrombosed vessels. Indeed, after its use one obtains very misleading pictures simulating vessel changes, which are in fact not present. See microscopic description of our case No. 20.

[3] Italics our own.

out the fact that we are not dealing with capillaries which have been changed into eosin-staining cords, but with vessels obliterated by a material which has all the morphologic and tinctorial properties of fibrin. Whenever these thrombi are not exceedingly dense and solid, it is easy to demonstrate vessel walls in thin sections which to all appearances are morphologically intact. It is generally also very easy to demonstrate this fact with reference to all vessels of the cortex, which are of a somewhat larger size, as well as to those of the medulla.

Duerck has just published an extensive contribution to the pathologic anatomy and histopathology of plague. In his summary of the microscopic changes he does not mention the thrombotic ones under discussion, but simply makes the following statement:

> The so-called parenchymatous organs, the liver and the kidneys, in all cases, even in those in which the disease has lasted a few days only, show those profound degenerative changes which are found also in other infectious diseases after a fatal issue. We see all degrees of cloudy swelling and beginning fatty degeneration. * * * In the kidneys, aside from the general toxic effect, the glomeruli appear to be the points especially vulnerable to the attacks of the plague virus. Even macroscopically one recognizes their enlargement and the great injection of the loops. Microscopic examination shows blood extravasation and epithelial desquamation, as well as the invasion of numerous plague bacilli. In six cases examined for this purpose the invasion of the glomeruli by plague bacilli was demonstrable. Occasionally this invasion leads to inflammatory changes combined with profound degeneration and hemorrhages, which produce, in the glomeruli especially, changes as we only find them in the most deleterious forms of post-scarlatinal or septic nephritis. (Table XV, figs. 29, 30, 31.)

The illustrations to which the author calls attention show hemorrhagic glomerulo-nephritis, but without any thrombosis. However, thrombotic processes are referred to in the description of case No. 14 in the following words:

> Almost all of the glomeruli are much enlarged, the capsules of Bowman dilated; the capillary loops, however, only partially fill the capsular space; they are generally reduced in size and partially obliterated by hyaline or leucocytic thrombi. Besides the loops in the capsular space, are found numerous red-blood corpuscles, mixed with desquamated capsular and reflected epithelia. * * * Homogeneous exudates are occasionally found in the capsules.

The preceding very recent contribution to the histopathology of plague does not do justice to the important thrombotic processes in

the kidney in this disease; nor does the description of Hamdi (who worked under Marchand) mention it at all. Hamdi had at his disposal material from seven plague cases and pieces of kidney from five. His description of the renal changes reads as follows:

> In our cases of plague the glomeruli vary in appearance. They are generally large, show many nuclei, and then fill the capsular space completely. Their capillaries are dilated and engorged with blood. Occasionally bacilli are diffusely distributed in these loops. In other cases, however, the glomeruli are small and the capillaries contain little blood. If this is the case and if the capillaries are collapsed, the capsular space contains a coagulated amorphous mass or a hyaline-like (*hyalinartige*) substance or blood, the latter being found also between the loops.

Since reporting the investigation of twenty cases of bubonic plague, and since becoming acquainted with the above-quoted publications, the writer has examined eleven more typical, fatal pest cases. We can now not only confirm our former statements as to renal vessel changes in plague but can further support them by additional observations and by additional staining methods employed in the investigation of the material.

The statement of Albrecht and Gohn, that the renal vessel changes which they have seen, but which they have misinterpreted, are to be found only in those cases in which numerous plague bacilli are circulating in the blood, we must contest, because our own investigation shows, as previously stated (Bulletin No. 23), that the presence or absence of bacterial metastatic emboli and the occurrence of hyaline fibrin thrombi do not entertain toward each other the relation of cause and effect. These two factors are indeed independent of each other, though they may be present simultaneously. A number of our cases demonstrate this beyond question. We saw very profound renal thrombotic processes without bacterial invasion and very extensive bacterial emboli in the absence of thrombi. Duerck likewise reports cases in which he speaks of the bacterial inundation of the kidneys without mentioning thrombosis. Of his case No. 7 he reports: "Everywhere in the capillary loops of the glomeruli and in other vessels numerous plague bacilli were found." Case No. 9: "Most glomeruli inundated by plague bacilli." Case No. 11: "Bacterial stains show an enormous inundation with plague bacilli; many glomeruli appear as if they had been injected with bacteria; likewise other renal vessels." In none of these cases are thrombotic processes proper mentioned.

However, so far as Duerck's case No. 11 is concerned, there is some suspicion that what this author describes as a bacterial injection of the vessels may indeed be a hyaline thrombosis. Such thrombi, in sections stained intensely with alkaline methylene blue, retain the blue and might, if densely fibrous in structure, be mistaken for crowded masses of bacteria.

ANALYSIS OF OUR 31 CASES.

An analysis of the 31 cases of plague examined by us shows that the total number comprises—

Group I. Primary uncomplicated bubonic plague	16
II. Primary bubonic plague with secondary plague septico-pyemia	7
III. Primary bubonic plague with secondary plague pneumonia	2
IV. Primary uncomplicated plague pneumonia	3
V. Primary pneumonia with secondary septico-pyemia	1
VI. Primary plague septicæmia	2
Total	31

Twenty-five of these were of the bubonic, four of the pneumonic, and two of the primary septic type. Of the bubonic cases there were—

Inguinal buboes	19
Axillary buboes	1
Cervical buboes	5

Of the total number of 31 cases there occurred in—

Native Filipinos	19
Chinese	11
Caucasians (native-born American)	1
Males	24
Females	7

According to age the distribution is as follows:

From 1 to 10 years	3
From 11 to 20 years	9
From 21 to 30 years	11
From 31 to 40 years	5
From 41 to 50 years	1
From 51 to 60 years	1
From 61 to 70 years	1
Total	31

Hyaline fibrin thrombi in the glomerular capillaries and in other renal vessels were found in cases Nos. 2, 11, 13, 14, 15, 16, 17, 18, 20, 23, 30, 31—that is, in 12 out of 31 cases, or in 38.71 per cent of the material investigated. These 12 cases are distributed among the six pathologic groups as follows:

Group.	Total number of cases.	Renal fibrin thrombi.	Percentage.
I. Primary uncomplicated bubonic plague	16	6	37.50
II. Primary bubonic plague with secondary plague septico-pyemia	7	4	57.14
III. Primary bubonic plague with secondary plague pneumonia	2		
IV. Primary uncomplicated plague pneumonia	3		
V. Primary pneumonia with secondary septico-pyemia	1		
VI. Primary plague septicæmia	2	2	100
Total	31	12	
Average per cent			38.71

The methods used in the histologic examination of our material were as follows:

Pieces of tissue from the plague bubo and from the internal organs in each case were immediately fixed in Zenker's solution during the autopsy. In a few cases other fixing fluids were used as a control, viz, Mueller's fluid, the Mueller-Orth formalin mixture, and others. Subsequently, the material was dehydrated in alcohol and embedded in paraffin. The sections were stained with hematoxylin-eosin, eosin-alkaline methylene blue, according to Weigert's fibrin method (preliminary carmin stain), Mallory's anilin-blue for connective tissue fibers, dilute carbol-fuchsin, and Wright's modification of Romanowski's stain. The best method in the study of the thrombotic processes in plague is furnished by Weigert's fibrin stain after fixation in Zenker's solution. Fixation in Flemming's solution or in Mueller's or Mueller-Orth's fluid is absolutely inadmissible for the study of the thrombotic processes. According to Disse the methods to be recommended in the fixation of renal tissues are very limited. Chromic acid and its salts, alcohol, and many other means frequently employed are inadmissible; but Zenker's solution, which acts like saturated corrosive sublimate, is to be recommended.

In all of the cases in which we found hyaline thrombi in the kidneys, sections were also stained by Van Gieson's method. The hyaline thrombotic material always stains yellow, never pink or

orange. The vessel walls themselves do not show any infiltration with a material staining pink or orange; hence a hyaline degeneration of the vessel wall in the strict sense of the term is not demonstrable. In fact, Van Gieson's stain is very well adapted to show the good state of preservation of the cellular elements of the vessel walls.

Sections from the 12 cases with renal thrombosis were further examined for amyloid. This was done because Duerck in his case No. 16 observed amyloid in the renal sections. However, the author does not attribute the presence of amyloid in this case to the pest infection, but to other chronic causes of long standing. We did not find amyloid material.

The following is an abstracted description of the 31 cases of human plague. A full description of 20 of these appeared in Bulletin No. 23. In the present report we are concerned exclusively with the presence or absence of hyaline-thrombi and of bacterial metastatic emboli in the renal tissue:

GROUP I. PRIMARY UNCOMPLICATED BUBONIC PLAGUE.

Case No. 1. Left Inguinal Bubo.

(Necropsy Protocol No. 1009. Postmortem examination July 27, 11 o'clock a. m., about eighteen hours after death, on the body of C. S., a male Chinese, 36 years old, from 217 Santo Cristo. Died July 26 at 4 o'clock p. m.)

Anatomical diagnosis.—Hypertrophy of the heart; congestion and fatty degeneration of the kidneys; fatty infiltration and degeneration of the liver; hemorrhagic inflammation and hypertrophy of the left inguinal, femoral, iliac, and retroperitoneal glands; hypertrophy, softening and congestion of the lymph glands in general; multiple subserous and submucous hemorrhages. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 2. Right Inguinal Bubo.

(Necropsy Protocol No. 989. T. C., a male Chinese, from Ilang Ilang Street, San Nicolas, 29 years of age. Died June 20, 1904. Postmortem examination nine hours after death.)

Anatomic diagnosis.—Hemorrhagic left inguinal bubo; general lymphadenitis; multiple hemorrhages into the serous and mucous membranes; congestion and parenchymatous degeneration of the kidneys; congestion and fatty degeneration of the liver; bubonic plague.

Microscopic examination.—In a majority of the glomeruli the capillaries are closed by hyaline fibrin thrombi, while here and there a Malpighian tuft is entirely free and nonoccluded. The

thrombi are generally solid, though some are distinctly tubular with an open lumen in the center. Occasionally one sees a thrombus extending from a Malpighian tuft into an afferent or efferent vessel, or even as far as an interlobular one. A few thrombi are also present in the small vessels of the medulla and likewise in the subcapsular glomeruli-free zone of the cortex. Changes of the vascular endothelium of the thrombosed vessels are not demonstrable. All through the renal tissue fairly numerous large bacilli, which retain Gram's stain, are found. These micro-organisms clearly represent a postmortem invasion frequently found in Manila in bodies upon which the postmortem examination can not be made immediately. Plague bacilli are not seen in the renal sections.

CASE NO. 3. LEFT INGUINAL BUBO.

(Necropsy Protocol No. 940. S. Y. S., male Chinese, 25 years old, from 70 Santo Cristo, Binondo. Ill six days. Died April 14, 1904, at 5.30 o'clock a. m. Postmortem examination six hours after death.)

Anatomic diagnosis.—Hypertrophy and hemorrhagic inflammation of the left inguinal and iliac glands; passive congestion and parenchymatous degeneration of the kidneys; congestion and œdema of the lungs; multiple subserous and submucous hemorrhages; moderate hypertrophy of the heart; old epicardial cicatrices; atheroma of the aorta; splenomegaly. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

CASE NO. 4. RIGHT INGUINAL BUBO.

(Necropsy Protocol No. 932. F. H., young male Filipino, from 20 Alma Street, Tondo. Died March 20, 1904, at 2 o'clock p. m. Postmortem examination made March 21 at 10 o'clock a. m., twenty hours after death.)

Anatomic diagnosis.—Large granulating ulcer on the right heel. Congestion and œdema of the lungs. Passive congestion of the liver and kidneys. Parenchymatous degeneration of the kidneys. Œdema, general hypertrophy, and congestion of the lymph nodes, particularly of those of the right inguinal region. Multiple subserous and submucous hemorrhages. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

CASE NO. 5. RIGHT INGUINAL BUBO.

(Necropsy Protocol No. 977. O. C., Chinese male, 25 years old, from 214 San Jacinto Street. Died after an illness of two days on May 25, 1904, at 9.15 p. m. Postmortem examination fifteen hours after death.)

Anatomic diagnosis.—Congestion of the lungs; congestion and parenchymatous degeneration of the kidneys; fatty degeneration of the liver;

multiple subserous and submucous hemorrhages; multiple hemorrhagic lymphadenitis. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any other renal vessels.

Case No. 6. Right Inguinal Bubo.

(Necropsy Protocol No. 998. Postmortem examination performed on July 3, 1904, twelve to eighteen hours after death, upon the body of V. D., from 17 Azcarraga Street, Tondo; a male Filipino, 17 years old.)

Anatomic diagnosis.—Congestion of the lungs; congestion and parenchymatous degeneration of the kidneys, splenomegaly, interstitial hepatitis with fatty degeneration, hemorrhagic lymphadenitis of the right inguinal glands. General hypertrophy and congestion of the lymph glands. Subserous and submucous hemorrhages. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 7. Right Inguinal Bubo.

(Necropsy Protocol No. 1000. July 5, 1905. Postmortem examination, thirty-nine hours after death, on the body of G. A., from No. 43 Valderama Street, San Nicolas; a Filipino boy about 10 years old.)

Anatomic diagnosis.—Hemorrhagic lymphadenitis of the right inguinal glands; multiple lymphadenitis with great congestion and softening; congestion of the kidneys and parenchymatous nephritis; fatty degeneration of the liver. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 8. Inguinal Bubo.

(Necropsy Protocol No. 965. R. F., native, female, 45 years old, from No. 33 Calle Victoria, Intramuros. Died May 7, 1904, at 11.45 o'clock p. m.; said to have been sick four days. Admitted to San Lazaro Hospital on May 7 at 11.30 o'clock p. m., and died fifteen minutes later. Postmortem examination eleven hours after death.)

Anatomic diagnosis.—Splenomegaly (primary?); perisplenitis; cirrhosis of the liver with moderate fatty degeneration; congestion and parenchymatous degeneration of the kidneys; congestion of both lungs; Banti's disease. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 9. Left Femoral Hemorrhagic Bubo.

(Necropsy Protocol No. 1081. A. M., male Filipino, 19 years old, from 352 Timbugan Street, Santa Cruz. Sick for two days. Died January 30, 1905. Postmortem examination thirty-two hours after death.)

Anatomic diagnosis.—Left femoral hemorrhagic bubo; multiple subserous and submucous hemorrhages; parenchymatous nephritis; congestion and œdema of the lungs. Bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

CASE NO. 10. LEFT INGUINAL AND FEMORAL HEMORRHAGIC BUBO.

(Necropsy Protocol No. 1115. O. K., male Chinese, 38 years old, from 84 Calle Nueva, Binondo. Died February 20, 1905, after an illness of a few days. Postmortem examination eighteen hours after death.)

Anatomic diagnosis.—Left inguinal and femoral hemorrhagic bubo; congestion of the lungs; acute parenchymatous nephritis; softening and enlargement of the spleen; bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

CASE NO. 11. RIGHT HEMORRHAGIC FEMORAL BUBO.

(Necropsy Protocol No. 1143. W. C., male Filipino, 53 years old, from No. 89 Lavezares Street, San Nicolas. Died March 18 at 1 o'clock p. m. Postmortem examination performed March 20, 1905, at 10 o'clock p. m.

Anatomic diagnosis.—Right hemorrhagic femoral bubo; hemorrhagic inflammation of the right iliac glands; congestion and œdema of the lungs; acute parenchymatous nephritis; enlargement of the spleen; bubonic plague.

Microscopic examination.—The thrombosis in the glomerular and other small renal vessels is of a rather moderate degree. A majority of the glomeruli (perhaps two-thirds in the sections examined) are free from thrombi. In these free Malpighian tufts we generally see a considerable number of dilated and engorged capillaries. No completely thrombosed glomerulus is found, but in those in which obliteration has occurred it is generally of a rather moderate, though occasionally of greater, extent. The thrombi are usually not very dense, but rather loose and incomplete, being composed of bands and strands and sometimes of reticula of fibrin. However, quite solid, dense, and uniformly homogeneous thrombi are likewise encountered, though not very frequently. In some of the glomerular and interlobular capillaries the incomplete obliteration depends merely upon the presence of a fine, wavy or angular filament of fibrin. However, the thrombosis, though of moderate degree, is not confined to the cortex; and small, more or less completely obliterated vessels are seen in the medulla. In the latter we see several longitudinally cut, dilated, and greatly engorged small veins, in which a considerable number of leucocytes and a few filaments of fibrin arranged longitudinally are present. More solid and more or less completely obliterating thrombi are likewise seen in the medullary vessels. *Morphological changes in the walls of either intra- or extra-glomerular vessels are not demonstrable.* Plague bacilli are not

seen anywhere in the renal sections, which, however, show diffuse invasion of the large cylindrical postmortem bacillus mentioned before. A study of the renal sections of this case shows clearly and unmistakably that the fibrin thrombosis is independent of any demonstrable morphologic vessel-wall changes. If such is found in advanced cases with extensive thrombosis, it is secondary to the primary obliteration.

There are present in some parts of the sections changes such as an increase of the connective tissue of the capsules of Bowman, fibrosis of the glomerulus, and increase of the interlobular connective tissue in general, which clearly point to an early chronic interstitial nephritis, which was present previous to the pest infection and entirely independent of it.

Case No. 12. Right Hemorrhagic Femoral Bubo.

(Necropsy Protocol No. 1150. S. H., 35 years old, male Chinese, from 119 La Coste Street, San Nicolas. Died March 24, 1905, 2 o'clock p. m. Postmortem examination made March 25 at 10 o'clock a. m.)

Anatomic diagnosis.—Right hemorrhagic femoral bubo; acute parenchymatous nephritis; multiple subserous and submucous hemorrhages; bubonic plague.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 13. Right Inguinal Bubo.

(Necropsy Protocol No. 1183. D. C., male Filipino, 19 years old, from 162 Barcelona Street, San Nicolas. Died May 12, 1905, at 6.30 p. m. Posmortem examination seventeen hours after death.)

Anatomic diagnosis.—Right inguinal, slightly hemorrhagic, bubo; congestion and œdema of the lungs; hemorrhagic parenchymatous nephritis; multiple subserous and submucous hemorrhages; congestion and œdema of the brain. Bubonic plague.

Microscopic examination.—Most of the glomeruli exhibit vessels obliterated by hyaline fibrin thrombi. In some of the Malpighian tufts the thrombosis is quite extensive, in others it is moderate, and in still others it is quite insignificant. However, glomeruli entirely free from obliteration are seen only rarely. Practically all of the thrombi encountered are made up of reticula and bands of fibrin. Completely solid and dense fibrin plugs in the glomerular vessels are not seen in this case. An extension of the thrombi into the afferent and efferent vessels occurs here and there. One also

occasionally sees a thrombus in an interlobular artery or in a vas rectum. The thrombotic processes are almost exclusively confined to the cortex, but a few thrombi are encountered in the medulla. The vessels of the latter are enormously dilated and engorged. The extreme glomeruli-free, subcapsular zone of the cortex does not contain any thrombi. Bacillar metastatic emboli are not found in the renal sections.

CASE No. 14. RIGHT CERVICAL BUBO.

(Necropsy Protocol No. 928. C. S., Filipino, age 5 years, from 170 Estero San Nicolas. Ill five or six days; three days in San Lazaro Hospital. Died March 18, 1904, at 11 o'clock p. m. Postmortem examination three hours after death.)

Anatomic diagnosis.—Perforating ulcer on the right side of the soft palate; general hypertrophy; congestion and hemorrhagic œdema of the general lymph glands of the body; œdema and congestion of the lungs; congestion and parenchymatous degeneration of the kidneys; œdema of the gall bladder wall; multiple subserous and submucous hemorrhages; syphilis hereditaria tarda. Bubonic plague.

Microscopic examination.—A moderate number of glomerular vessels show hyaline (fibrin) thrombi. Nowhere is this thrombosis very extensive or at all complete; it affects only a minor part of the vessels of one glomerulus. The renal vessels in general are very much congested, and a very few areas of blood extravasation are found. The few bacilli which are visible are found in connective tissue lymph clefts or in the capsular space of a glomerulus, but not inside of blood vessels.

CASE No. 15. CERVICAL BUBO.

(Necropsy Protocol No. 910. C. S., a Filipino girl, 9 years of age, from Anda Street, Intramuros, Manila. Postmortem examination five hours after death, on Saturday, March 5, 1904, at 4 o'clock p. m.)

Anatomic diagnosis.—Hemorrhagic, acute, parenchymatous nephritis; congestion and œdema of the lungs; moderate fatty degeneration of the liver; hemorrhagic inflammation, hypertrophy and softening of the cervical glands on both sides; more or less general hypertrophy of most of the lymph glands. Bubonic plague.

Microscopic examination.—The renal tissue presents a most striking picture. Sections from both kidneys, treated by Weigert's fibrin method, appear as if the vessels had been injected with a violet-stained gelatin. There is not a normal glomerulus to be seen. All the sections show a more or less complete obliteration by hyaline thrombi. In most of the Malpighian bodies the hyaline

thrombosis of the capillaries is so perfect that both the main branches of the afferent vessel and the smaller capillaries given off from the larger loops are sharply outlined. Some of the thrombi appear perfectly solid; others are hollow in the center, as can be seen both in transverse and in longitudinal sections; and still others are made up of fibers and filaments. The endothelial lining of the thrombosed vessels is well preserved. Where the thrombi are comparatively thin, one can see, both in transverse and in longitudinal sections, endothelia which are apparently perfectly normal. Nowhere do the thrombosed vessels show a loss of endothelia to any extent. Therefore, the thrombosis can not be attributed to a denudation of the vessels of their endothelial lining. The capsules of Bowman are likewise normal, though a few of them show a very moderate degree of thickening; their lining epithelium exhibits no marked changes. In some places the hyaline thrombi are continued not only into the vasa afferentia but even into the interlobular arteries. Quite commonly there are seen between the uriniferous tubules parts of such small vessels filled with hyaline thrombi. However, none are found in the larger arteries or veins, in some of which finely granular fibrin and desquamated endothelial cells are present. The vessel walls themselves show no damage aside from a minor degree of denudation of the intima. There is in particular no extension of the fibrin through the vessel walls, nor is there any evidence of mesophlebitic or periphlebitic or arteritic processes. Nowhere do any of the renal blood vessels show a large number of bacilli; a few are possibly seen inside some vascular lumina, but even these are not definite. A moderate number of bacilli are seen in the lymph clefts between the tubules and around the Malpighian bodies. A few slender, long bacilli, which retain Gram's stain, are occasionally found in the tubules; they represent a postmortem invasion.

CASE NO. 16. RIGHT INGUINAL BUBO.

(No necropsy protocol kept. Male Chinese, 26 years old, who died after an illness of seven days.)

Microscopic examination.—Sections of the kidneys show hyaline fibrin thrombosis of the glomerular capillaries, with an extension into the afferent and efferent vessels as well as into the intertubular capillaries and small veins. There is general vascular dilatation and engorgement of the renal vessels.

GROUP II. PRIMARY BUBONIC PLAGUE WITH SECONDARY PLAGUE SEPTICO-PYEMIA.

Case No. 17. Right Inguinal Bubo with Secondary Plague Septico-Pyemia.

(Necropsy Protocol No. 1011. M. N., male Filipino, 40 years old, from 77 Sacristia Street, San Nicolas. Ill six days; died early July 29, 1904. Postmortem examination about six hours after death.)

Anatomic diagnosis.—Congestion and œdema of the lungs; hemorrhagic, acute, parenchymatous nephritis; parenchymatous and fatty degeneration of the liver; hemorrhagic inflammation of the right inguinal and many other lymph glands; extensive subserous, submucous, and interstitial hemorrhages. Bubonic plague; plague septico-pyemia.

Microscopic examination.—All the renal vessels, including the glomerular capillaries, are much dilated and engorged. Hyaline fibrin thrombi are found in a few of the glomeruli. The thrombosis of the glomerulus is, as a rule, not complete and only a part of the tuft is closed by fibrin. The thrombi are sometimes continued into the vasa afferentia and efferentia and beyond them. A few thrombi are also present in the vasa recta of the medulla. The capsular epithelium shows a minor degree of degenerative, but no proliferative, change. Sections from the kidneys show an extensive infection with plague bacilli, which is mostly localized in the glomerular capillaries. Both in the open and in the thrombosed capillaries numerous bacilli may be seen in loose groups or sometimes even in dense masses. In the thrombosed vessels the bacilli are sometimes between the thrombus and the vessel wall. The organisms occasionally extend beyond the glomerulus into the vasa interlobulares. Here and there, bacilli are found at quite a distance from a glomerulus and occasionally in the capsular space and in the uriniferous tubules.

Case No. 18. Left Femoral Hemorrhagic Bubo.

(Necropsy Protocol No. 1127. G. P., male Chinese, 35 years old, from 182 Calle Camba. Died March 6, 1905. Postmortem examination performed three hours after death.)

Anatomic diagnosis.—Left femoral hemorrhagic bubo; acute hemorrhagic nephritis; fatty degeneration of the liver. Bubonic plague; plague septico-pyemia.

Microscopic examination.—The thrombosis of the glomerular capillaries in this case is very extensive—in fact, it is found in every glomerulus in the numerous sections examined. In general the

obliteration of the capillaries is not complete, most of the thrombi being of the tubular variety, with an open lumen in the center. However, there are also seen many perfectly solid and dense, completely obliterating thrombi. In a fair number of places the fibrin thrombi in the glomeruli are of such size that they have greatly distended the vessels in the transverse diameter and stretched them in a longitudinal direction, so that they have a sausage-like appearance. The afferent and efferent vessels frequently show an incomplete thrombosis in the shape of an open fibrin reticulum. This network may be continued into the main branches of the afferent vessel and is occasionally found even in the finest glomerular capillaries. Here and there, but rarely only, one sees fibrin filaments which have penetrated through the vessel wall into the perivascular tissue. From the afferent vessels the thrombosis can sometimes be followed into the arteriæ interlobulares. On the other hand, thrombi are likewise found in the small interlobular capillaries, into which the vasa efferentia break up. In the subcapsular glomeruli-free zone, in terminal branches of arteriæ interlobulares which do not supply glomeruli, and in interlobular capillaries of such arteries, as also in small branches of the stellate veins, obliterating fibrin plugs are likewise encountered. It is thus seen that almost all of the smaller vessels of the cortex are affected by the process of fibrin thrombosis. However, all of the different sets of vessels are not involved to the same extent, the greatest amount of obliteration being found in the glomerular capillaries and in their afferent and efferent vessels. In the medulla and also in the medullary rays the extent of the thrombosis is quite moderate, when compared with that which is seen in the cortex, but here and there one observes a thrombosed smaller vein, artery, or capillary. However, the much-engorged capillary network surrounding the straight tubules is almost without exception free from fibrin.

It is difficult and often impossible to study the endothelial lining in those vessels in which the thrombi are quite dense, solid, and have completely obliterated the lumina. Where this is not the case—where we are dealing with thinner tubular wall thrombi or with fibrin reticula, or even with solid thrombi which have become somewhat shrunken or retracted—one can generally see well-preserved, apparently unchanged, vascular endothelia. In somewhat larger vessels the muscle fibers present a normal appearance. Mallory's special stain shows the delicate fibers of the glomerular

as well as the other vessels. Neither the capsular nor the reflected glomerular epithelia show any proliferative changes.

Loose groups of plague bacilli are found here and there in the small renal vessels and also in the uriniferous tubules.

CASE No. 19. LEFT HEMORRHAGIC INGUINAL BUBO.

(Necropsy Protocol No. 1132. A. A., male Filipino, 17 years old, from 75 Principe Street, San Nicolas. Died March 7, 1905, p. m. Postmortem examination made on March 8, twelve hours after death.)

Anatomic diagnosis.—Left hemorrhagic inguinal bubo; parenchymatous nephritis; multiple subserous and submucous hemorrhages. Bubonic plague; plague septico-pyemia.

Microscopic examination.—The microscopic examination does not show any hyaline glomerular thrombosis, but metastatic bacterial emboli are found in these structures. Here and there a hyaline cylinder is seen in a tubule. (These hyaline casts do not give the tinctorial fibrin reaction.)

CASE No. 20. LEFT HEMORRHAGIC INGUINAL BUBO.

(Necropsy Protocol No. 1157. T. B., a female Filipina, 21 years old, wife of a Chinese from Lavazares Street, San Nicolas. Died March 31, 1905. Postmortem examination made April 1, a. m.)

Anatomic diagnosis.—Left hemorrhagic inguinal bubo; hemorrhagic inflammation of the left pelvic, iliac, and retroperitoneal glands; hemorrhagic parenchymatous nephritis; œdema and congestion of the lungs and also of the brain; uterus gravis, menses I to II; bubonic plague and plague septico-pyemia.

Microscopic examination.—This is one of the cases in which very extensive thrombotic processes in the kidneys, particularly in the glomerular vessels, are present. Here we find perfectly solid, heavy, completely obliterating thrombi, tubular wall thrombi with an open lumen in the center, and also loose fibrin reticula, the latter especially in the vasa efferentia. In the glomerular vessels which are not completely, but only partly, thrombosed, an œdematous or homogeneous swelling of the vessel wall is noticeable. The glomerular epithelium shows proliferative changes, the nuclei within the glomeruli are decidedly increased in number, and the Malpighian corpuscles as a whole appear quite solid with little or no open capsular space left.

Thrombi are comparatively scanty in the subcapsular glomeruli-free zone, in the medulla, and in the medullary rays. In one glomerulus, in which the capillaries contain both fibrin thrombi and bacterial emboli, a peculiar condition is seen. Watery fluid had

evidently forced its way between the capsule proper and the epithelial lining of the former. The capsular epithelium in a complete intact layer had become desquamated, and a cyst, lined on one side by over one-half of the capsule proper and on the other side by the capsular epithelium, had compressed the Malpighian tuft into one corner of the capsular space. The tuft with its thrombosed capillaries is seen as a compressed, somewhat crescent-shaped mass in one extremity of the capsule opposite the cyst.

The kidneys show an extensive infection by metastatic emboli, composed of dense or loose masses of plague bacilli. These are found in the glomerular vessels, in the intertubular capillaries, and in small arteries and veins. Interglomerular vessels sometimes show both hyaline fibrin thrombi and bacterial emboli, but the number of the latter is very much smaller than that of the former. In other words, we see hyaline thrombi in almost all of the glomerular capillaries, but bacterial invasion only here and there. Bacilli are also found in the perivascular and in the interlobular lymph spaces. The thrombotic processes are evidently independent of the bacterial invasion, and much of the latter in this case is undoubtedly due to postmortem growth, since the kidneys as well as all organs show numerous large, cylindrical, Gram-staining bacilli, which are commonly found in Manila in necropsies which are made a considerable time after death.

It might also be mentioned here that in sections fixed by Zenker's fluid and stained according to Weigert's fibrin method, plague bacilli often retain the gentian violet. That this is indeed the case may be confirmed by the use of other stains and by comparing alternating sections of short series. In sections from blocks of tissue fixed in the Mueller-Orth mixture the fibrin has lost its characteristic tinctorial reaction, and when treated by Weigert's method it appears so hazy that it is entirely unrecognizable, neither its homogeneous hyaline appearance nor its fibrous character in other places showing well. If such sections, from material fixed in Mueller formalin, are stained with hematoxylin and eosin, the obliterated glomerular vessels do not furnish a clear picture. The boundaries of the thrombi are indistinct and the coagula appear continuous with the vessel walls. The latter themselves create the impression of being in a state of swelling and hyaline degeneration. Sections fixed in corrosive-sublimate solution and colored with a variety of stains, including carmin-Weigert, eosin-methylene-blue,

Van Gieson, Mallory, etc., clearly show that a hyaline degeneration of the vessel walls does not exist, but is one simulated by the faulty method of fixation.

A somewhat superficial examination of the placenta in this case failed to show any invasion by the plague bacillus. This result is in accord with the observation of the German Plague Commission on several fœti from females dead from plague.

Case No. 21. Left Submental Bubo.

(Necropsy Protocol No. 1027. F. C., a Filipina, 14 years old, from 195 Plaza Leon XIII, Tondo. Died after a short illness of unknown duration on September 7, 1904, at 7.10 o'clock p. m. Postmortem examination made on September 8 at 3 o'clock p. m.)

Anatomic diagnosis.—Congestion and parenchymatous degeneration of the kidneys; congestion and œdema of the lungs; one necrotic focus of the liver with congestion and fatty degeneration; multiple subserous and submucous hemorrhages; left submental hemorrhagic bubo. Bubonic plague and plague septico-pyemia.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 22. Right Cervical Bubo with Secondary Plague Septico-Pyemia.

(Necropsy Protocol No. 889. E. J., a male Filipino, 63 years old, from 142 Caballeros Street, San Nicolas. Died February 18, 1904, at 1 o'clock p. m. Ill five days; cause of death unknown. Postmortem examination made February 19 at 8.45 o'clock a. m., about twenty hours after death.)

Anatomic diagnosis.—Congestion and œdema of the lungs; congestion and parenchymatous degeneration of the kidneys; subserous and submucous hemorrhages; right cervical bubo. Bubonic plague and plague septico-pyemia.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 23. Right Axillary Bubo.

(Necropsy Protocol No. 973. F. A., male Filipino, age 28 years, from 661 Calle Bilibid, Santa Cruz. Died May 9, 1904, at 11 o'clock p. m. Postmortem examination made fifteen hours after death.)

Anatomic diagnosis.—Congestion and œdema of the lungs; parenchymatous degeneration of the kidneys; right axillary hemorrhagic bubo; general swelling, hypertrophy, and congestion of the lymph glands. Bubonic plague and plague septico-pyemia.

Microscopic examination.—In the kidneys all the vessels are much dilated and engorged, particularly the glomerular capillaries. Here and there in the glomeruli an incomplete fibrin thrombosis is met

with. Groups of plague bacilli are found in the glomerular and intertubular vessels, some of them amounting to fairly dense masses of bacteria. A very few isolated bacilli are seen here and there in the uriniferous tubules.

GROUP III. PRIMARY BUBONIC PLAGUE WITH SECONDARY PLAGUE PNEUMONIA.

Case No. 24. Ambulatory Plague, terminating by Embolism of the Pulmonary Artery. Inguinal Bubo.

(Necropsy Protocol No. 901. Filipino, male, 17 years old, from 185 Misericordia Street. Died February 27, 1904, at 2 o'clock p. m. Postmortem examination thirteen hours after death.)

Anatomic diagnosis.—Congestion and œdema of the lungs; parenchymatous degeneration of the kidneys; embolism of the pulmonary artery; inguinal buboes. Bubonic plague and plague pneumonia.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

Case No. 25. Left Hemorrhagic Femoral Bubo.

(Necropsy Protocol No. 1141. A. L., male Filipino, 19 years old, from 101 Principe Street, San Nicolas. Died March 16, 1905, p. m. Postmortem examination performed March 17, 1905, twenty hours after death.)

Anatomic diagnosis.—Left hemorrhagic femoral bubo; small lobular focus in the lower lobe of the right lung; general pulmonary congestion and œdema; enlargement and softening of the spleen, congestion of the kidneys, and parenchymatous nephritis; bubonic and pneumonic plague. (Smears from the pulmonary lobular focus show numerous plague bacilli, as do also smears from the bubo and from the spleen.)

Microscopic examination.—In this case the kidneys do not show any hyaline thrombosis or any metastatic bacterial emboli, but, without regularity as to distribution, all through the tissues is found the cylindrical postmortem bacillus before mentioned. An interesting pathologic change seen in this case is a proliferation of the glomerular epithelium. The proliferated capsular epithelium proper on the inner surface of Bowman's capsule forms crescentic masses, which frequently fill out the capsular space. The reflected epithelium is likewise increased and the glomerular vessels are greatly dilated and engorged.

GROUP IV. PRIMARY UNCOMPLICATED PLAGUE PNEUMONIA.

Case No. 26. Primary Uncomplicated Plague.

(Necropsy Protocol No. 970. A. Q., Chinese, male, 30 years old, a shopkeeper from 67 Tetuan Street, Santa Cruz. Ill six days. Died May 18, 1904, at 10.30 o'clock p. m. Postmortem examination made thirteen hours after death.)

Anatomic diagnosis.—Parenchymatous degeneration of the kidneys; fatty

and parenchymatous degeneration of the liver; multiple subserous and submucous hemorrhages; lobular pneumonia of the right lung. Plague pneumonia.

Microscopic examination.—No hyaline thrombi found in the glomerular capillaries or in any of the other renal vessels.

Case No. 27. Primary Uncomplicated Plague Pneumonia.

(Necropsy Protocol No. 971. C. C., Chinese, male, 27 years old, from 67 Tetuan Street, Santa Cruz. Ill six days. Died May 18, 1904. Postmortem examination fourteen hours after death.)

Anatomic diagnosis.—Parenchymatous degeneration of the kidneys and liver; multiple subserous and submucous hemorrhages; pneumonia; acute adhesive fibrinous pleurisy. Plague.

Microscopic examination.—No hyaline thrombi are found in the glomerular capillaries or in any of the other renal vessels.

Case No. 28. Plague Pneumonia.

(Necropsy Protocol No. 1116. J. W. H., male, American (Caucasian), 28 years old, from Intramuros. Died February 20, 1905, after an illness of two days. Postmortem examination fifteen hours after death.)

Anatomic diagnosis.—Lobular pneumonia of the right lower lobe; great congestion and œdema of both lungs; acute parenchymatous nephritis; fatty degeneration of the liver.

Microscopic examination.—No hyaline thrombi in the glomerular capillaries or in any of the other renal vessels.

GROUP V. PRIMARY PLAGUE PNEUMONIA WITH SECONDARY PLAGUE SEPTICO-PYEMIA.

Case No. 29. Primary Plague Pneumonia with Secondary Septico-Pyemia.

(Necropsy Protocol No. 962. F. S., Filipina, female, 30 years old, from 148 Anda Street, Intramuros, Manila. Died May 7, 1904, at 5.30 p. m. Cause of death unknown. Plague suspected. Postmortem examination made sixteen hours after death.)

Anatomic diagnosis.—Lobular pneumonic foci; congestion and beginning diffuse red hepatization of both lower lobes; general congestion of the lungs; subpleural hemorrhages; congestion and parenchymatous degeneration of the liver and kidneys; submucous hemorrhages in the gastric and intestinal mucosa; hemorrhagic endometritis; microcystic degeneration and congestion of the left ovary. Plague pneumonia and septicæmia.

Microscopic examination.—The most striking histologic change in the kidneys are metastatic emboli in the glomerular capillaries, completely filling some of the loops of the tufts. However, such

emboli are found in a limited number of glomeruli only; nor are any tufts seen where all the capillaries are obliterated. The embolic closure is generally confined to one lobe of a glomerulus. Sometimes the embolic bacterial mass extends into the afferent or efferent vessel (it is impossible to decide which of the two is affected). In the neighborhood of such thrombosed vessels there are small microscopic areas of blood extravasation, in which few bacilli are found. All the renal vessels are much engorged, particularly the small vessels, and the interstitial tissue is quite œdematous. Small microscopic areas of blood extravasation are encountered all through the sections. A few bacilli are often seen in such areas as well as in the tubules, the lymph clefts, and even occasionally in the small arteries and veins. The tubular epithelium shows profound cloudy swelling and fatty degeneration. Hyaline fibrin thrombi are not present in the renal tissue.

GROUP VI. PRIMARY PLAGUE SEPTICÆMIA.

Case No. 30. Primary Plague Septicæmia.

(Necropsy Protocol No. 983. L. T. T., Chinese, male, 28 years of age, from 211 Santo Cristo Street, San Nicolas. Ill for ten days. Died June 4, 1904, at 1 o'clock p. m. Postmortem examination made fifteen hours after death.)

Anatomic diagnosis.—Congestion and œdema of the lungs; fatty degeneration of the liver; acute parenchymatous nephritis; multiple subserous and submucous hemorrhages (lungs, heart, kidneys, ureters, bladder, stomach, intestines). Plague septicæmia.

Microscopic examination.—The histologic changes in the kidneys are very profound. There is universal cloudy swelling and fatty degeneration of the tubular epithelium. The tubules are generally filled with granular detritus, and in many instances sharply outlined hyaline casts are found. These hyaline masses are composed of a homogeneous material (staining with eosin and somewhat with methylene blue); however, this does not give the tinctorial fibrin reaction. The glomerular capillaries are generally not much altered, but here and there a partial hyaline (fibrin) thrombosis can be seen. Occasionally one observes an intertubular thrombosed vessel. Plague bacilli are found in small groups in some of the glomeruli; they are also observed both in the capillaries and between them. A very few isolated organisms are encountered in the interstitial connective tissue between the tubules.

CASE NO. 31. PRIMARY PLAGUE SEPTICÆMIA.

(Necropsy Protocol No. 1082. T. B., Filipina, female, 13 years of age, from 346 Cabildo Street, Intramuros. Ill two days. Died January 30, 1905. Postmortem examination made twenty-four hours after death.)

Anatomic diagnosis.—Multiple subserous and submucous hemorrhages; parenchymatous nephritis; congestion and œdema of the lungs. Plague septicæmia. (Smears from the spleen, which is moderately enlarged, show many plague bacilli; those from the liver, the kidneys, and the glands show a few.)

Microscopic examination.—Some capillary loops in a few glomeruli and some extraglomerular vessels show hyaline fibrin thrombi. Loose, isolated groups of plague bacilli are found in the tubules, the capsular spaces, and the renal blood vessels.

SUMMARY OF OBSERVATIONS ON THE VASCULAR CHANGES IN THE KIDNEYS.

Upon reviewing the results of the examination of 12 cases in which hyaline fibrin thrombi were found in the glomerular capillaries and in other renal vessels, we arrive at the following general conclusions:

The thromboses may be of a moderate degree and may be found only in a small proportion of the renal vessels; or they may be of a most extensive character, involving a large number. In general it may be stated that the thrombosis is always most profound in the cortex, and much less so in the medulla. However, the latter is never entirely free. As a rule, to which none of our cases were an exception, the thrombosis is always most profound in the glomerular capillaries and in the afferent and efferent vessels. Next in order of frequency stand the interlobular vessels and the intertubular capillaries of the cortex. In case of a moderate thrombosis, only a few of the glomerular capillaries are occluded. The rest are free and are then generally more or less engorged with blood; however, they occasionally may be empty and collapsed, but great engorgement of the renal vessels is generally the rule in plague. In more severely affected cases a greater proportion of the glomerular vessels is occluded, and the afferent and efferent vessels are likewise obliterated. In the ones where the highest degree of thrombosis occurs, it may be difficult to find a single glomerulus in which this has not occurred to a greater or less extent. In such cases thrombi are in fact present in all the different sets of vessels of both cortex and medulla. We find them in the subcapsular glomeruli-free zone, in

the capillaries, and in the terminal branches of the interlobular arteries. They are seen in the glomerular capillaries, the afferent and efferent vessels, the interlobular arteries, and the intertubular capillaries of the cortex. In such cases we also find quite a number of vasa recta of the medulla obliterated. In favorable sections we may occasionally be able to follow the thrombosis from a larger artery into the smaller branches and into the capillaries. The thrombi vary much in degree of density. We may encounter perfectly solid, heavy ones, which even in the thinner sections appear as hyaline structureless masses, which have greatly extended the vessel and stretched it, both in a transverse and in a longitudinal direction, so that it appears very much like a sausage contained in a thin skin; or, on the other hand, we may find tubular wall thrombi with open lumina in the center, or a solid thrombus, which, however, does not completely fill the vessel, but leaves a circular lumen between itself and the vessel wall. We also see thrombi which are distinctly fibrous in structure, being composed of longitudinally and reticularly arranged filaments. Or again, we encounter thrombi made up of a very loose reticulum. The vessel walls, as a rule, show no appreciable morphologic changes. The intima and its endothelium are well preserved, and in the small arteries we see well-preserved muscle fibers. However, if the thrombi are quite solid and dense, then the vessel walls generally show a minor degree of injury, and their cellular structural elements can not be clearly distinguished. In most of the cases in which we found hyaline thrombi in the renal vessels, bacterial emboli were not encountered. However, in other instances, such emboli are present either as dense bacterial masses or as loose groups of plague bacilli. In such cases in one place in the section there may be seen a bacterial embolism and in another a hyaline thrombosis, and occasionally one may encounter thrombi and invading bacteria in the same area. But it is perfectly clear, as a careful examination will reveal, that the bacterial invasion is not the cause of the thrombus formation, because the latter, as a rule, occurs quite independently of the former. Among our 31 cases there are instances with profound thrombosis but without bacterial invasion of the kidneys, and on the other hand, of extensive metastatic bacterial emboli without hyaline thrombi. As a general rule, where we find extensive hyaline thrombosis in the primary bubo and in the spleen, we also encounter it in the kidneys.

We have asked ourselves: Where in the kidneys do the vascular thrombotic processes begin and how do they spread? We are unable to give an entirely satisfactory answer to this question. It is evident that the glomerular capillaries and the afferent and efferent vessels are most generally and most profoundly involved, but even where we find in these sets of vessels only a very moderate involvement, we also find at least some fibrin obliteration in the capillaries of the tubuli contorti, which are the branches of the vasa efferentia. It appears quite probable that the process begins in the glomerular capillaries and spreads simultaneously along the afferent and efferent tracts, reaching the interlobular arteries of the former and the vasa recta spuriæ of the latter. In both mild and severe cases of renal thrombosis some thrombi are also found in the medulla and in the medullary rays, in places quite remote from the glomeruli. Here there probably occur some foci of the thromboses, which arise independently of the earliest ones in the glomerular capillaries. We are firmly of the opinion that the formation of the renal hyaline thrombi occurs independently of the presence of the plague bacillus and that it is due to toxines of this micro-organism circulating in the blood, but exactly how these toxines give rise to the thrombus formation is a question which we are at present unable to answer. Very probably they may have a deleterious influence upon the vascular endothelium, but certainly they do not ordinarily produce a manifest, demonstrable morphologic change either in the intima or in the renal vessel walls in general.

According to the intensity of the process, the 12 cases in which thrombosis in the renal vessels was encountered may be divided into three groups, viz:

Thrombosis of a moderate degree: Cases Nos. 11 (1143), 14 (928), 17 (1011), 23 (973), 30 (983)—5 cases.

Thrombosis of a higher degree: Cases Nos. 2 (989), 13 (1183), 16, 31 (1082)—4 cases.

Thrombosis of a very high degree: Cases Nos. 15 (910), 18 (1127), 20 (1157)—3 cases.

Extensive and frequently occurring hyaline fibrin thrombosis of the glomerular capillaries and of the other renal vessels has not often been found in human infectious diseases, at least not in a high percentage of the larger series of cases examined, and in animal diseases only in the example cited by Welch (swine plague).

A review of the literature on the subject of glomerular thrombosis was published in Bulletin No. 23.

CONCLUDING REMARKS.

In conclusion we wish to emphasize again the frequent occurrence of renal hyaline fibrin thrombosis in bubonic plague. We have found this histopathologic change in nearly 40 per cent of our cases, viz, in seven out of the first series of twenty and in five out of the second series of eleven. As the familiarity of the observer with this condition increases, his ability of finding it macroscopically becomes greater. In those cases in which we find very profound thrombosis, this process probably extends over the entire cortex; but in those of moderate intensity it is found, it appears, only here and there throughout the cortical tissue. Therefore in such cases as the latter one must be critical in the selection of the microscopic material. Quite generally the congestion and engorgement of the kidneys in plague is very great, and the enlarged glomeruli stand out as dark-red points on a contrasting background of cloudy and grayish-yellow convoluted tubules, but the glomeruli obliterated by fibrin thrombi themselves assume a granular, shining, grayish-white appearance, and they may, after a little practice, easily be recognized with the naked eye.

Our plague material, which is in no way an exceptional one, but on the contrary an average typical collection of cases, justifies the conclusion that plague in man is, among all human diseases in general, the one in which highly characteristic hyaline thrombotic processes in the glomeruli and in the renal vessels at large are most frequently encountered. These important processes have heretofore not been sufficiently considered, wrongly interpreted, and generally have been altogether overlooked. In the literature of plague a hyaline degeneration of the vessel walls in the kidneys and in other organs is frequently mentioned, but, as pointed out by the author in this publication and in previous ones, we are not concerned at all with such a condition, but with primary hyaline thrombotic processes presenting in the elements of the vessel wall themselves only occasional and comparatively very insignificant secondary degenerations. Likewise in the plague bubo we are generally encountering primarily a true hyaline thrombosis, and only later, after general tissue necrosis in consequence of enormous bacterial invasion, do we find extensive degeneration and complete necrosis of the vessel walls.

It is of course impossible to derive any enlightenment as to the initial changes in the vessels from the profoundly necrotic tissue of the plague bubo, as the condition encountered represents the final product of a most destructive process. The kidneys form a much more favorable material for the study of the initial changes in the vessel in the thrombotic processes, because death occurs before such profound alterations as are found, as a rule, in the original plague bubo take place.

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LIST OF ILLUSTRATIONS.[1]

FIGURE 1. Thrombosis of interlobular and afferent vessel and of interglomerular capillaries. A bend, cut transversely, indicates the place where the afferent vessel is given off from the interlobular one. From case No. 15 (910).

2. Thin, filamentous fibrin thrombus in the afferent vessel of a glomerulus. From case No. 2 (989).

3. Thrombosed glomerulus. Section stained with Mallory's connective-tissue anilin-blue stain. Tubular wall thrombi and connective tissue framework are shown. From case No. 18 (1127).

4. Heavy, dense thrombi in the interlobular capillaries of the cortex. (Branches of the efferent vessels between the tubuli contorti.) From case No. 15 (910).

5. Loose thrombus in the intertubular capillaries of the cortex. (Branches of the efferent vessel between the tubuli contorti.) From case No. 20 (1157).

6. 7. Fibrin network in the afferent vessel of a glomerulus at the entrance into the latter. From case No. 20 (1157).

8. Tubular wall thrombi in the interglomerular capillaries. From case No. 18 (1127).

9. Artery and branch in cortex, completely obliterated by a heavy, dense thrombus. In the longitudinally cut artery some endothelial and muscle cells are shown. From case No. 18 (1127).

10. Heavy thrombus in an interlobular artery. Vessel wall well preserved. From case No. 18 (1127).

11. Loose, fibrous thrombus in an interlobular vessel of the cortex, showing a well-preserved normal vessel wall. From case No. 18 (1127).

12. Cyst formation in a glomerulus with compression of the thrombosed tuft. From case No. 20 (1157).

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[1] All the illustrations are photomicrographs prepared by the aid of a large Zeiss camera from paraffin-embedded sections, fixed in Zenker's fluid and stained with carmine and Weigert's gentian-violet, unless otherwise stated. The objectives used were DD and homogenous oil immersion, 2 millimeters; aperture 1.40, and projection ocular No. 4. Length of bellows of camera, generally 35 centimeters.

FIGURE 13. Loose thrombus in a terminal branch of an interlobular artery in the glomeruli-free subcapsular zone of the cortex. Vessel wall normal. From case No. 20 (1157).

14. Fibrin network in a vein in the medulla. From case No. 11 (1143).

15. Heavy, dense tortuous thrombus in a vein in the medulla. From case No. 18 (1127).

16. Heavy thrombi in the vasa recta of the medulla. From case No. 15 (910).

17. Bacterial embolism in a capillary of the medulla. From case No. 18 (1127).

18. Bacterial embolism and fibrin thrombus in an interglomerular vessel cut transversely. Eosin and methylene-blue stain. *a*, Bacterial embolism; *b*, Fibrin thrombus. From case No. 18 (1127).

19. Fibrin network and bacterial embolism in an afferent vessel just at the entrance into the glomerulus. Eosin and methylene-blue stain. *a*, Bacterial embolism; *b*, Fibrin network. From case No. 20 (1157).

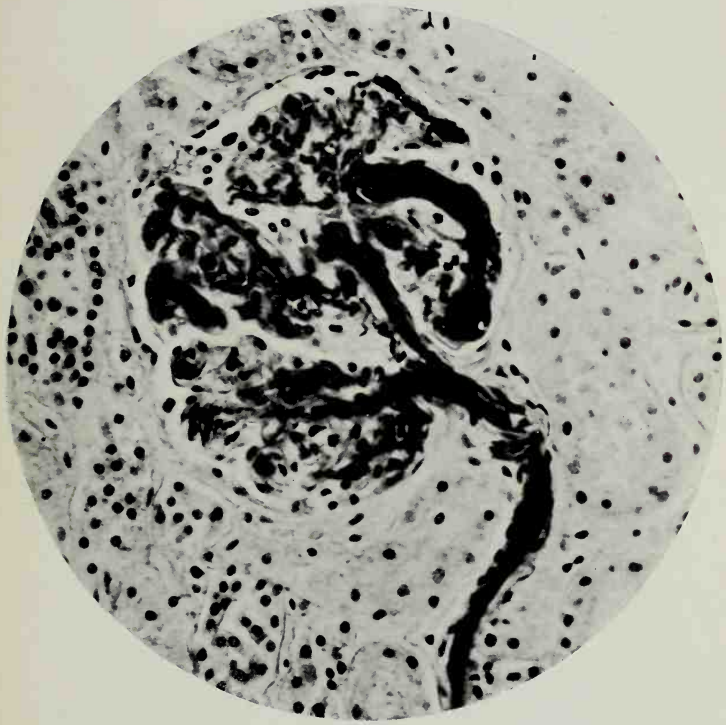


FIG. 1.

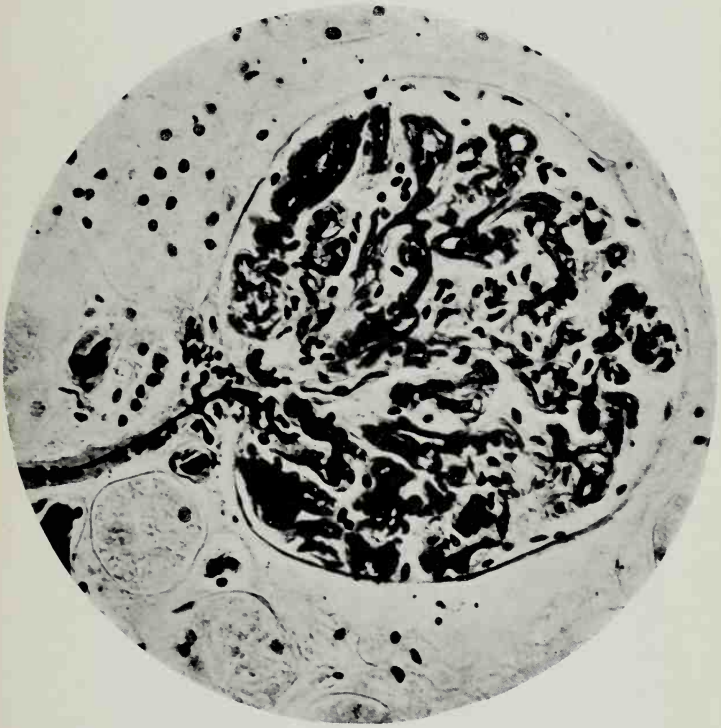


Fig. 2.

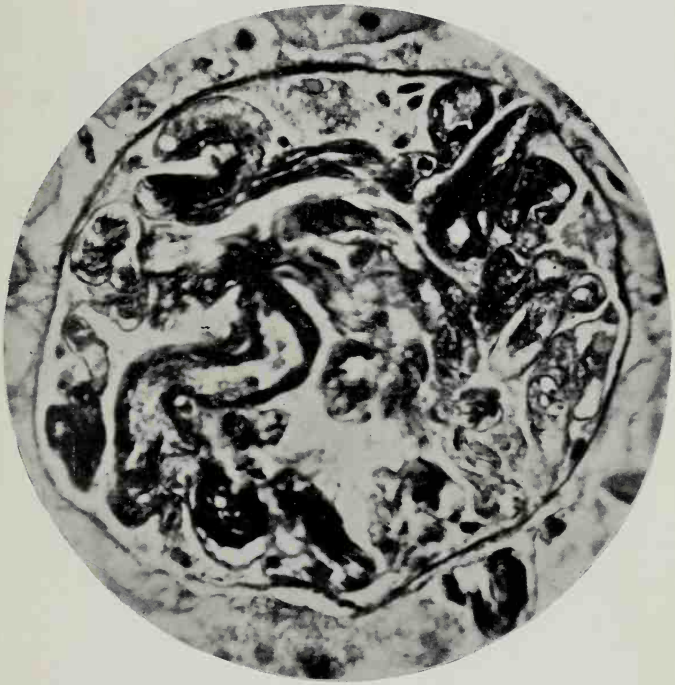


FIG. 3.

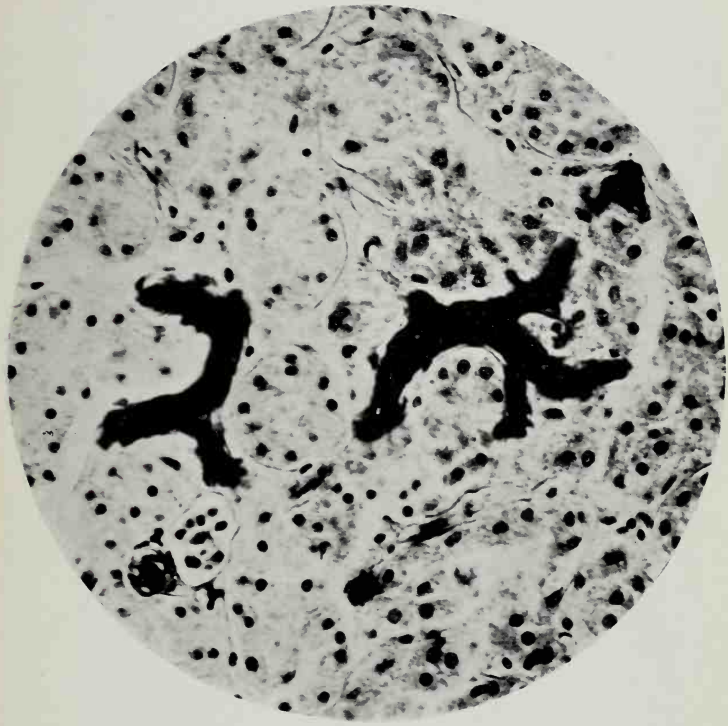


Fig. 4.

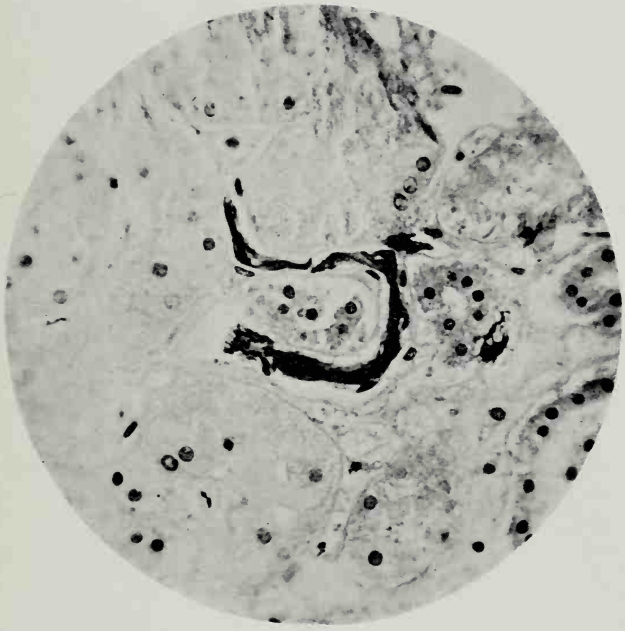
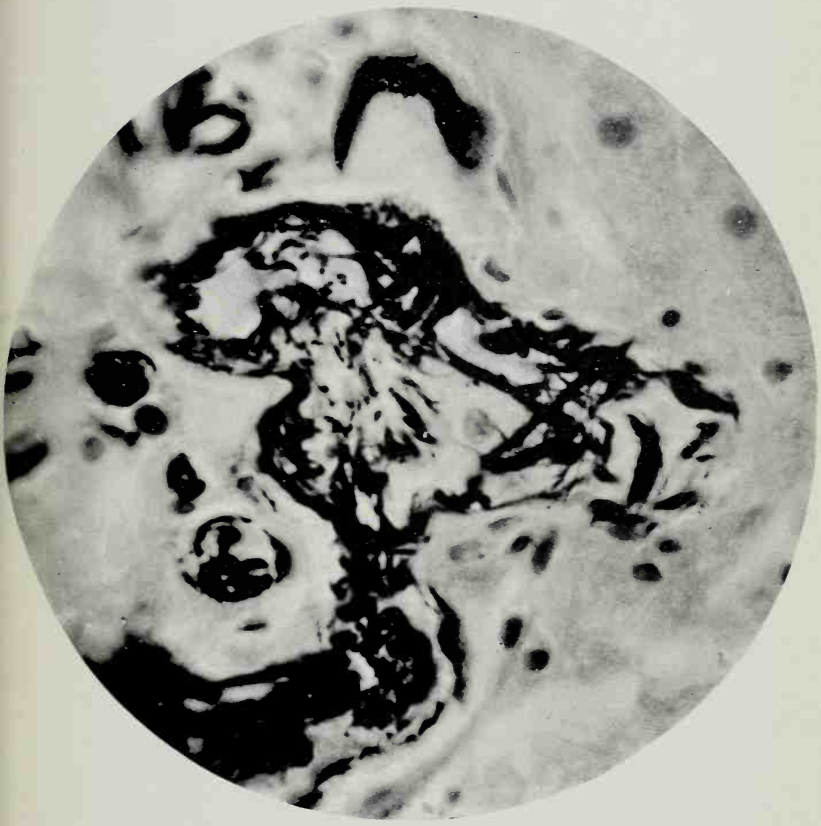


Fig. 5.

FIG. 6.



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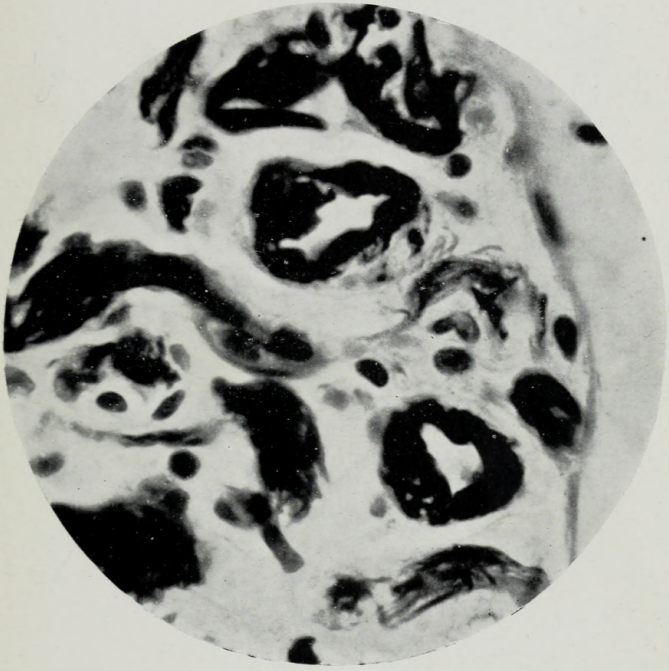

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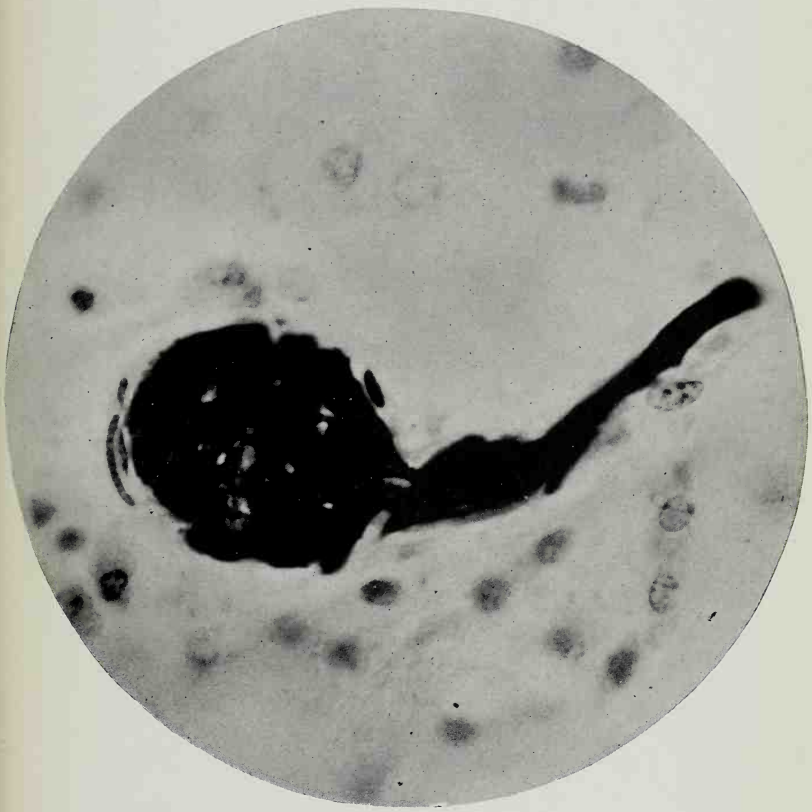

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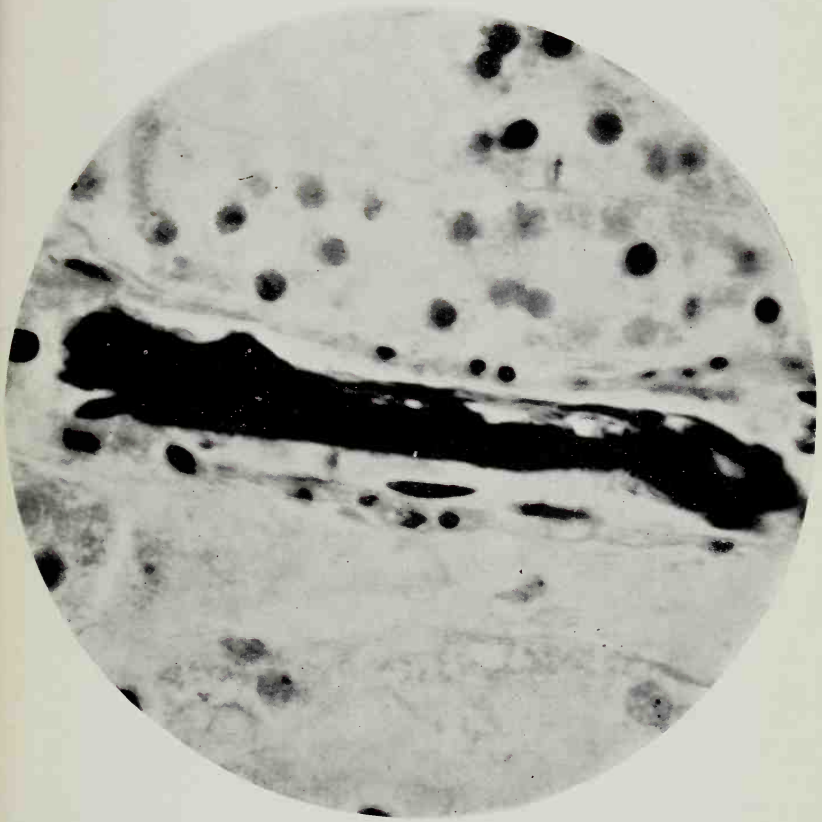


Fig. 10.

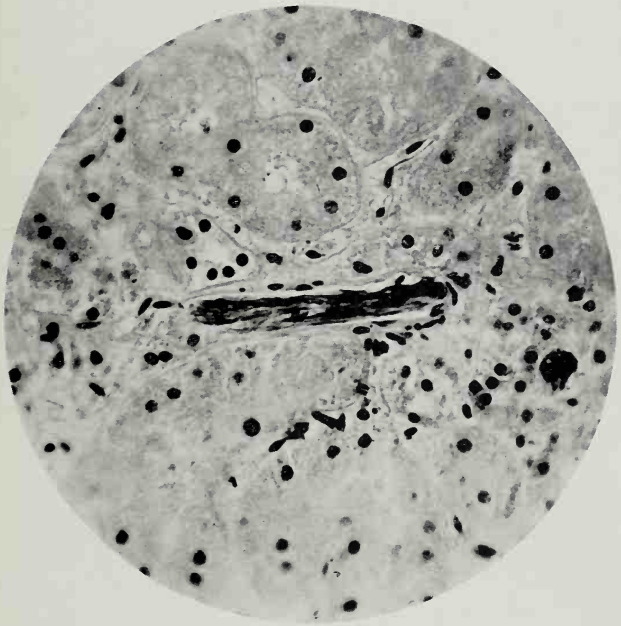


FIG. 11.

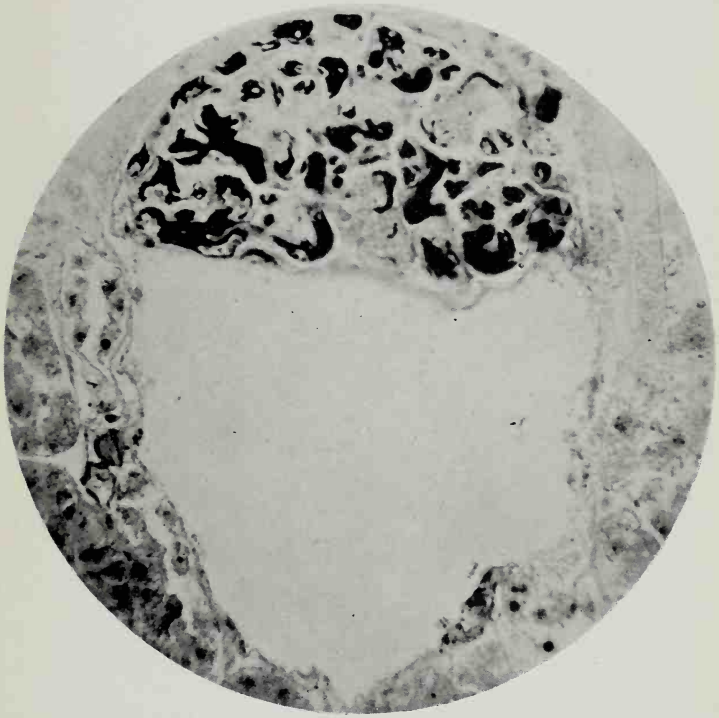


FIG. 12.

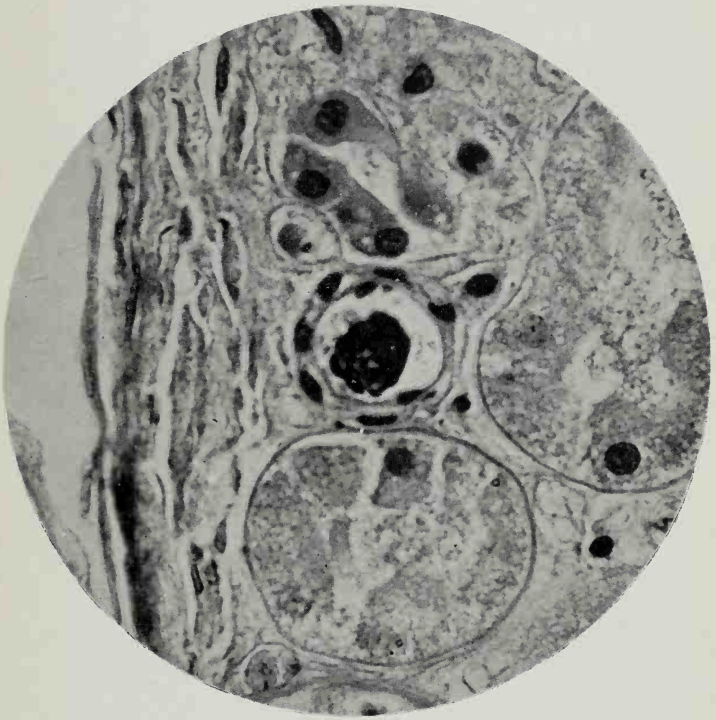


Fig. 13.

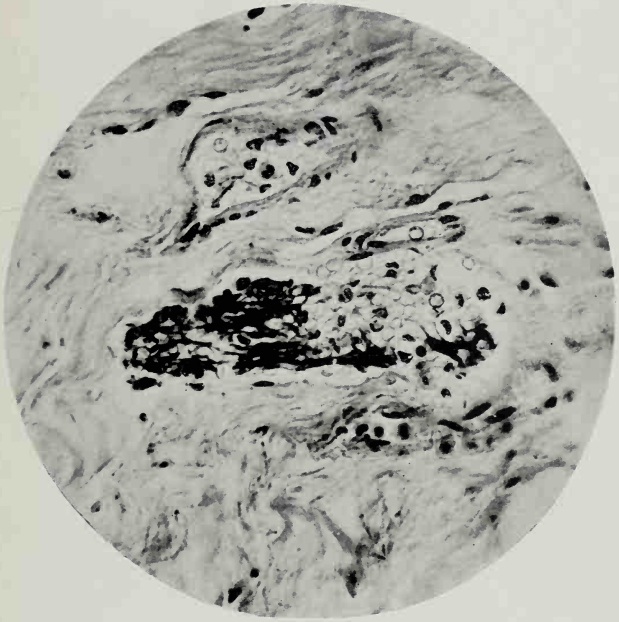


FIG. 14.

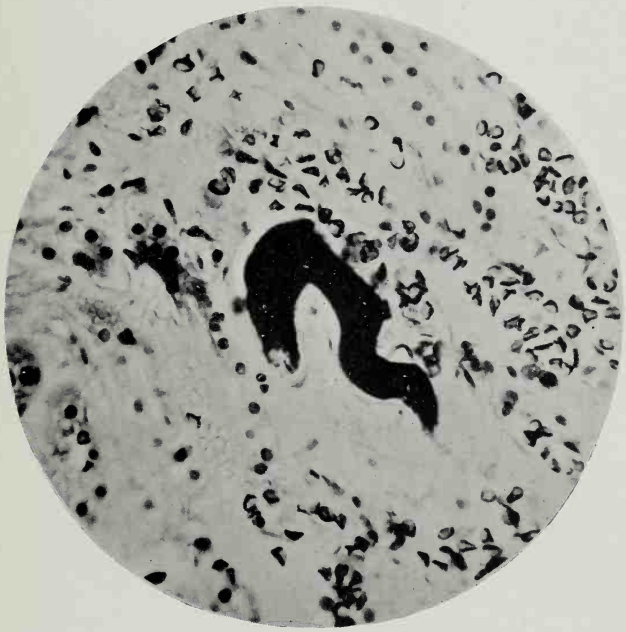


Fig. 15.

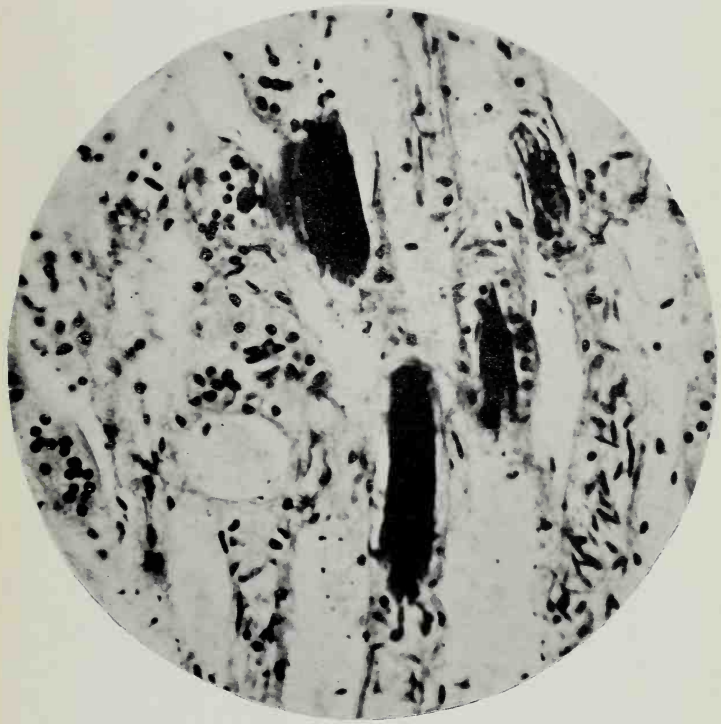
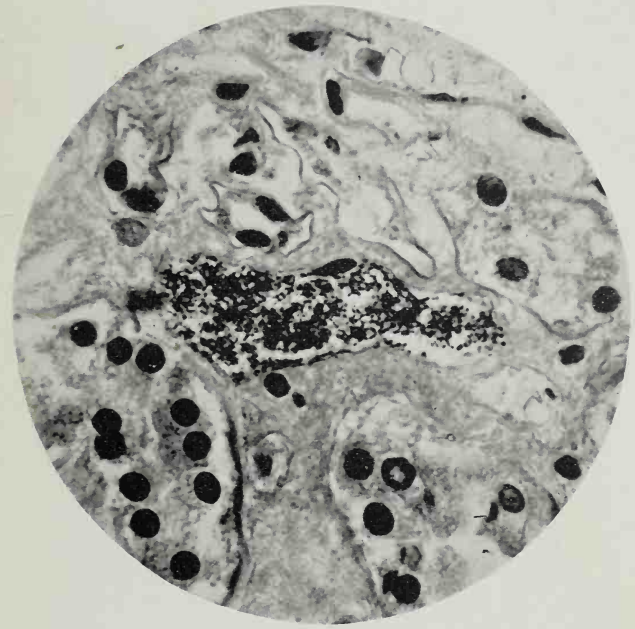


Fig. 16.



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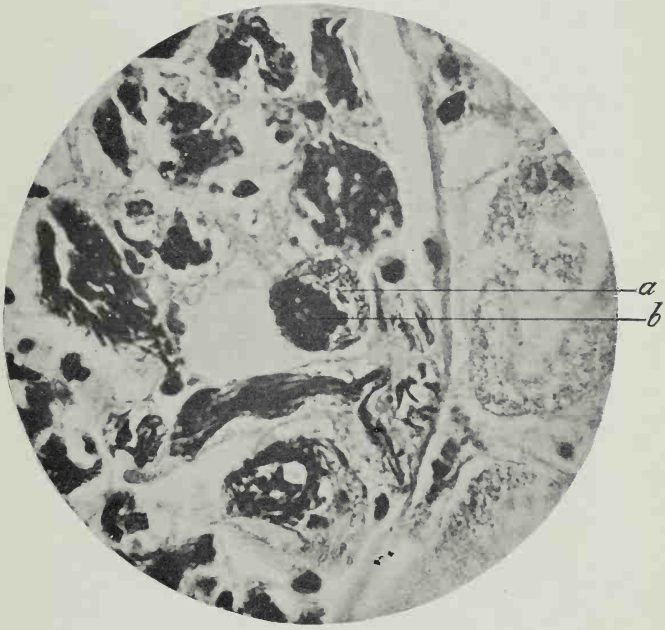

FIG. 18.

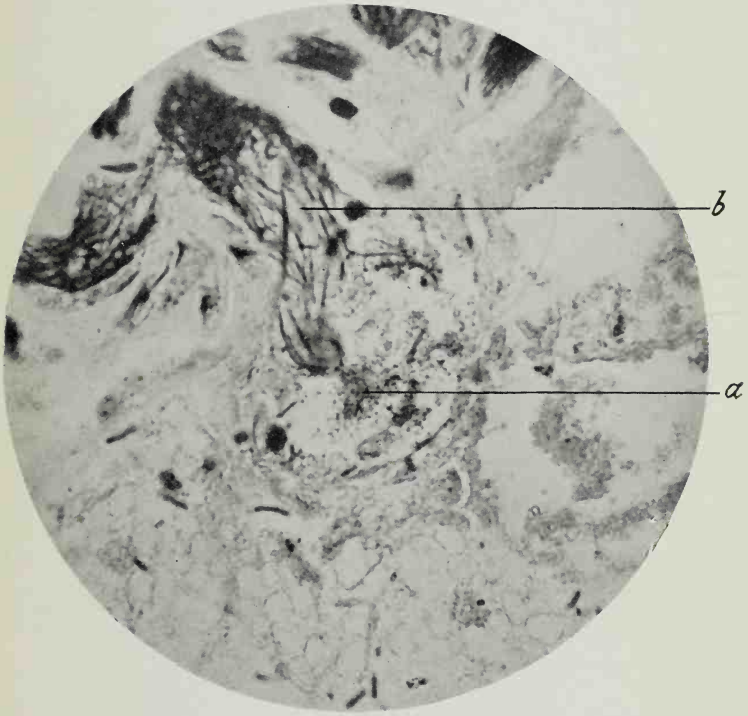

FIG. 19.

Herzog, M.

Further observations on fibrin thrombosis in the glomerular… vessels in bubonic plague.